

IDIOPATHIC MALE INFERTILITY IS RELATED WITH GAMETOGENESIS GENES EXPRESSION: RESULTS BY A FUNCTIONAL ANALYSIS OF GENE ONTOLOGY TERMS.

N Garrido, JA Martinez-Conejero, J Jauregui, R Sharma, JA Horcajadas, J Remohi, A Pellicer, M Meseguer, Introduction: Sperm analysis based in sperm count and motility has been employed for the diagnosis of male fertility for several decades. It is an useful tool to determine the fertile status of a male. There are still a significant number of infertile males where their sperm features, as determined by the basic sperm analysis are normal. Recent investigations have described the relevance of sperm mRNA in fertilization and early embryo development. Microarray technology informs about a wide range of mRNAs expression within a single experiment, and is ideal to analyze sperm expression profiles (SEP) in cells or tissues. Bioinformatic helps in the organization of such amount of results by following logical processes of gene expression grouping. Our aim with this work was to compare the SEP in spermatozoa obtained from males with idiopathic infertility versus those from sperm donors of proven fertility by employing microarray technology followed by a functional analysis, in order to determine the biological processes in male fertility that are different in infertile vs. fertile males. Methods: Sperm samples were obtained from infertile males (n=5) presenting normal sperm count and motility (WHO criteria) parameters and donors (n=5) of proven fertility. Sperm mRNA was extracted using Trizol protocol, suspended in DEPC-treated water and frozen at -80 until the microarray experiments were performed in duplicate. Results: Several groups of genes exhibit a significantly different proportion of the genes over or underexpressed in infertile males versus fertile sperm donors. In a different analysis level, different biochemical pathways or processes are implicated. Interestingly, when over or underexpressed genes in infertile males were grouped by their function, those involving spermatozoa differentiation were present at all analysis levels. Spermatid development, gametogenesis, spermatid differentiation, and male gamete generation processes present between 80-100% of their genes with a significant over expression in donors in comparison with infertile males showing normal sperm count. This suggests that infertility markers that may not be related with sperm production in terms of sperm count, but related with sperm function. Conclusions: When the results of a differential microarray analysis between fertile and infertile males on spermatozoa are organized into functionally similar clusters, several biochemical or differentiation pathways are altered, but mainly those involved in male gamete formation. This is unequivocal evidence about the existence of several molecular infertility factors independent from the total sperm production. Microarray based sperm analysis is a promising diagnostic tool of male infertility, that needs to be further explored.